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Customer No.:

Docket No: 3940/0K188

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Michael Friedman et al.

Serial No.: 09/534,960 Art Unit: 1615

Confirmation No.: 3862

Filed: March 27, 2000 Examiner: S. Lee Howard

For: CONTROLLED DELIVERY SYSTEM OF ANTIFUNGAL AND KERATOLYTIC AGENTS FOR LOCAL TREATMENT OF FUNGAL INFECTIONS OF THE NAIL AND SURROUNDING TISSUES

PENDING CLAIMS FOR SERIAL NO. 09/534,960

ACCOMPANYING RESPONSE TO OFFICE ACTION DATED 6/17/02

47. (Amended) A sustained release therapeutic nail varnish composition comprising:

(a) an antifungal effective amount of an antifungal agent;

(b) a keratolytic agent in an amount sufficient to increase permeability of the nail;

(c) greater than 3% (w/w) of a humectant to trap water;

(d) water in an amount sufficient to hydrate the nail and thereby to increase permeability of the nail in combination with said keratolytic agent;

(e) a polymeric film forming agent selected to form a sustained release film upon application of said composition on a nail and evaporation of said volatile solvent; and

(f) a volatile solvent;

said sustained release film configured to trap water from said composition and maintain it in contact with said nail, said water and said humectant in combination facilitating penetration of said antifungal agent into the nail, and thereby enhancing therapeutic effectiveness of said antifungal agent.

48. The nail varnish of claim 47, wherein said antifungal agent is selected from the group consisting of amphothericin B, butefanine, butoconazole, carbol-fuchsin, ciclopirox, clioquinol, clotrimazole, econazole, gentian violet, ketoconazole, miconazole, naftifine, nystatin, oxiconazole, sodium thiosulfate, terbinafine, terconazole, tolnaftate, undecylenic acid, therapeutically acceptable salts thereof, derivatives thereof and mixtures thereof.

49. The nail varnish of claim 48, wherein said antifungal agent is clotrimazole or miconazole nitrate.

50. The nail varnish of claim 47, wherein said antifungal agent is present in an amount of less than about 1% of the total weight of the composition.

51. (Amended) The nail varnish of claim 47, wherein said antifungal agent is present in an amount of less than about 5% of the total weight of the composition excluding said volatile solvent.

52. The nail varnish of claim 47, wherein said keratolytic agent is selected from the group consisting of urea, sulfur, salicyclic acid, podophyllum resin and mixtures thereof.

53. The nail varnish of claim 47, wherein said keratolytic agent is urea.

54. The nail varnish of claim 47, wherein said keratolytic agent is present in an amount of less than about 1% of the total weight of the composition.

55. (Amended) The nail varnish of claim 47, wherein said keratolytic agent is present in an amount of from about 0.05% to about 5% of the total weight of the composition excluding said volatile solvent.

56. The nail varnish of claim 47, further comprising an antibacterial agent, an antiviral agent, an antipsoriatic agent or mixtures thereof.

57. The nail varnish of claim 56, wherein said antibacterial agent is selected from the group consisting of bacitracin, clindamycin, erythromycin, gentamicin, mupirocin, neomycin, tetracyclines, polymyxin B, benzalkonium chloride, boric acid, hexachlorophene, iodine, iodoquinol, mafenide, mercury ammoniated, metronidazole, nitrofurazone, selenium sulfide, silver sulfadiazine, salts thereof, derivatives thereof and mixtures thereof.

58. The nail varnish of claim 56, wherein said antibacterial agent is present in an amount of from about 0.01% to about 1% of the total weight of the composition.

59. (Amended) The nail varnish of claim 56, wherein said antibacterial agent is present in an amount of from about 0.05% to about 5% of the total weight of the composition excluding said volatile solvent.

60. The nail varnish of claim 56, wherein said antiviral agent is selected from the group consisting of acyclovir, amantadine, cidofovir, famciclovir, foscarnet, ganciclovir, palivizumab, penciclovir, ribavirin, rimantadine, valcyclovir, salts thereof, derivatives thereof, and mixtures thereof.

61. The nail varnish of claim 56, wherein said antiviral agent is present in an amount of from about 0.08% to about 0.8% of the total weight of the composition.

62. (Amended) The nail varnish of claim 56, wherein said antiviral agent is present in an amount of from about 0.8% to about 8% of the total weight of the composition excluding said volatile solvent.

63. The nail varnish of claim 56, wherein said antipsoriatic agent is selected from the group consisting of alclometasone, amcinonide, betamethasone, clobetasol, clocortolone, desonide, desoximetasone, diflorasone, fluocinolone, fluocinonide, flurandrenolide, halcinonide, hydrocortisone, mometasone, prednicarbate and triamcinolone, salts thereof, derivatives thereof, and mixtures thereof.

64. The nail varnish of claim 56, wherein said antipsoriatic agent is present in an amount of from about 0.02% to about 2% of the total weight of the composition.

65. (Amended) The nail varnish of claim 56, wherein said antipsoriatic agent is present in an amount of from about 0.1% to about 10% of the total weight of the composition excluding said volatile solvent.

66. The nail varnish of claim 47, wherein said humectant is selected from the group consisting of glycerol, sorbitol and mixtures thereof.

67. The nail varnish of claim 47, wherein said humectant is present in an amount of from about 3% to about 15% of the total weight of the composition.

68. (Amended) The nail varnish of claim 47, wherein said humectant is present in an amount of from about 5% to about 35% of the total weight of the composition excluding said volatile solvent.

69. The nail varnish of claim 47, wherein said water is present in an amount of less than about 5% of the total weight of the composition.

70. (Amended) The nail varnish of claim 47. wherein said water is present in an amount of from about 0.4% to about 25% of the total weight of the composition excluding said volatile solvent.

71. The nail varnish of claim 47, wherein said polymeric film forming agent is selected from the group consisting of hydrophobic polymers.

72. The nail varnish of claim 71, wherein said hydrophobic polymer is selected from the group consisting of hydrophobic cellulose derivatives, hydrophobic methacrylic polymers, cellulose acetate phthalate, shellac, derivatives thereof, and mixtures thereof.

73. The nail varnish of claim 72, wherein said hydrophobic cellulose derivative is selected from the group consisting of ethyl cellulose of any acceptable molecular weight.

74. The nail varnish of claim 72, wherein said hydrophobic methacrylic polymer is selected from the group consisting of methacrylic acid copolymer type B (USP/NF), methacrylic acid copolymer type C (USP/NF), ammonio methacrylate copolymer type B (USP/NF) and ammonio methacrylate copolymer type A (USP/NF), derivatives thereof, and mixtures thereof.

75. The nail varnish of claim 47, wherein said polymeric film forming agent is present in an amount of less than about 7.5% of the total weight of the composition.

76. (Amended) The nail varnish of claim 47, wherein said polymeric film forming agent is present in an amount of from about 8% to about 35% total weight of the composition excluding said volatile solvent.

77. The nail varnish of claim 47, wherein said polymeric film-forming agent is present in a weight ratio of polymer to antifungal agent from about 1:0.01 to about 1:0.3.

78. The nail varnish of claim 47, wherein said polymeric film-forming agent is present in a weight ratio of polymer to keratolytic agent from about 1:0.01 to about 1:1.

79. The nail varnish of claim 47, wherein said polymeric film-forming agent is present in a weight ratio of polymer to antibacterial agent from about 1:0.01 to about 1:0.3.

80. The nail varnish of claim 47, wherein said polymeric film-forming agent is present in a weight ratio of polymer to antiviral agent from about 1:0.02 to about 1:0.2.

81. The nail varnish of claim 47, wherein said polymeric film-forming agent is present in a weight ratio of polymer to antipsoriatic agent from about 1:0.006 to about 1:0.15.

82. (Amended) The nail varnish of claim 47, further comprising a plasticizer.

83. The nail varnish of claim 82, wherein said plasticizer is selected from the group consisting of dibutyl sebacate, diethyl phthalate, lanolin alcohols, mineral oil, petrolatum, polyethylene glycol, propylene glycol, triacetin, triethyl citrate, and mixtures thereof.

84. The nail varnish of claim 82, wherein said plasticizer is present in an amount of from about 0.1% to about 2% of the total weight of the composition.

85. (Amended) The nail varnish of claim 82. wherein said plasticizer is present in an amount of from about 0.5% to about 10% of the total weight of the composition excluding said volatile solvent.

86. The nail varnish of claim 82, wherein said plasticizer is present in a weight ratio of plasticizer to polymer from about 0.04:1 to about 0.3:1.

87. The nail varnish of claim 47, wherein said volatile solvent is selected from the group consisting of an alcohol, a ketone, and mixtures thereof.

88. The nail varnish of claim 87, wherein said alcohol is selected from the group consisting of ethanol, isopropyl alcohol, methanol and mixtures thereof, and further wherein said ketone is acetone.

89. The nail varnish of claim 47, wherein said volatile solvent is a mixture of acetone and isopropyl alcohol.

90. The nail varnish of claim 47, wherein said volatile solvent is present in an amount of from about 60% to about 90% of the total weight of the composition.

91. The nail varnish of claim 89, wherein said acetone and said isopropyl alcohol are present in a volumetric ratio of acetone to isopropyl alcohol from about 1:4 to about 4:1.

92. The nail varnish of claim 47, wherein said solvent system further includes at least one

non-volatile solvent selected from the group consisting of benzyl alcohol, benzyl benzoate, corn oil, cottonseed oil, ethyl oleate, glycerin, glycofural, isopropyl myristate, isopropyl palmitate, mineral oil, peanut oil, polyethylene glycol, propylene glycol, propylene carbonate, sesame oil, soybean oil, water, and mixtures thereof.

93. (Amended) A method of preparing a sustained release therapeutic varnish formulation, comprising the steps of:

(a) preparing a solution comprising water and a volatile solvent;

(b) adding water to the solution prepared in (a);

(c) dissolving a keratolytic agent and an antifungal agent into the solution prepared in (b);

(d) adding an humectant to the solution prepared in (c); and

(e) dissolving a polymeric film forming agent in the solution prepared in (d); said film forming agent being selected so as to form a sustained release film upon application of the formulation on a nail and evaporation of said volatile solvent, said sustained release film configured to trap water in contact with the nail and the surrounding tissues.

94. Cancelled.

95. The sustained release therapeutic nail varnish composition of claim 47 further comprising an excipient.

96. (Amended) A sustained release therapeutic nail varnish composition comprising:

(a) an antifungal effective amount of an antifungal agent;

(b) a keratolytic agent in an amount sufficient to increase permeability of the nail;

(c) a humectant to trap water;

(d) a polymeric film forming agent;

(e) water; and

(f) a volatile solvent; wherein upon application on a nail, the volatile solvent evaporates and a sustained release film coating forms on the surface of the nail, the sustained release film coating releasing the antifungal and keratolytic agents in respective effective amounts over a prolonged period of time and trapping water in contact with the nail; the humectant retaining water in the film; and said keratolytic agent and said water increasing permeability of the nail surface and facilitating penetration of the released antifungal agent below the nail surface.

97. The sustained release therapeutic nail varnish composition of claim 96 further comprising an excipient.

98. (New) A method of treating a fungal infection comprising administering to a subject a therapeutically effective amount of a sustained release therapeutic nail varnish composition, wherein the composition comprises:

(a) an antifungal amount of an antifungal agent;

(b) a keratolytic agent in an amount sufficient to increase permeability of the nail;

(c) greater than 3% (w/w) of a humectant to trap water in a film;

(d) water in an amount sufficient to hydrate the nail and thereby to increase permeability of the nail in combination with said keratolytic agent;

(e) a polymeric film forming agent; and

(f) a volatile solvent; said film forming agent being selected so as to form a sustained release film upon application of said composition on a nail of said subject and evaporation of said volatile solvent, said sustained release film configured to trap water from said composition and maintain it in contact with said nail, said water and said humectant in combination facilitating penetration of said antifungal agent into the nail, and thereby enhancing effectiveness of said antifungal agent.

99. (New) The method of claim 93 said formulation being suitable for application by spraying.